

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.usplo.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,980	12/17/2001	David Dolphin	273012010901	1219
			EXAMINER	
23220	& FOERSTER LLP		NOGUEROLA, ALEXANDER STEPHAN	
3811 VALLEY	CENTRE DRIVE		ART UNIT	PAPER NUMBER
SUITE 500 SAN DIEGO.	CA 92130-2332		1753	
,			DATE MAILED: 02/11/200	4

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)				
	10/026,980	DOLPHIN ET AL.				
Office Action Summary	Examiner	Art Unit				
	ALEX NOGUEROLA	1753				
The MAILING DATE of this communication	appears on the cover shee	t with the correspondence address				
Period for Reply						
A SHORTENED STATUTORY PERIOD FOR RETHE MAILING DATE OF THIS COMMUNICATION - Extensions of time may be available under the provisions of 37 CF after SIX (6) MONTHS from the mailing date of this communication - If the period for reply specified above is less than thirty (30) days, and if NO period for reply is specified above, the maximum statutory period for reply within the set or extended period for reply will, by some Any reply received by the Office later than three months after the meaned patent term adjustment. See 37 CFR 1.704(b).	NN. R 1.136(a). In no event, however, ma i. a reply within the statutory minimum of striod will apply and will expire SIX (by	ay a reply be timely filed of thirty (30) days will be considered timely. MONTHS from the mailing date of this communication. DECREAN DONED (35 U.S.C. § 133).				
Status		<i>:</i>				
1) Responsive to communication(s) filed on _	•					
2a) This action is FINA 2b)	This action is FINAL 2b)⊠ This action is non-final.					
Since this application is in condition for all	Since this application is in condition for allowance except for formal matters, prosecution as to the merits is					
closed in accordance with the practice und	ler Ex parte Quayle, 1935	C.D. 11, 453 O.G. 213.				
Disposition of Claims						
4)⊠ Claim(s) <u>1-21</u> is/are pending in the applica	ation.					
4a) Of the above claim(s) is/are with	ndrawn from consideration	l.				
5) Claim(s) is/are allowed.						
6)⊠ Claim(s) <u>1-21</u> is/are rejected.						
7) Claim(s) is/are objected to.						
8) Claim(s) are subject to restriction a	ind/or election requiremen	t.				
Application Papers						
9) ☐ The specification is objected to by the Exa	miner.					
10\☑ The drawing(s) filed on 17 December 200	1 is/are: a)⊠ accepted or	b) objected to by the Examiner.				
Applicant may not request that any objection t	o the drawing(s) be held in al	beyance. See 37 CFR 1.05(a).				
Replacement drawing sheet(s) including the c	orrection is required if the dra	awing(s) is objected to. See 37 CFR 1.121(u).				
11) The oath or declaration is objected to by the	ne Examiner. Note the atta	ached Office Action of John 1 10-132.				
Priority under 35 U.S.C. § 119						
12) Acknowledgment is made of a claim for fo	reign priority under 35 U.S	S.C. § 119(a)-(d) or (f).				
a)∏ All b)∭ Some * c)∭ None of:						
1 Certified copies of the priority docu	ments have been received	d.				
2. Certified copies of the priority docu	ments have been received	In Application No				
3. Copies of the certified copies of the	e priority documents have	been received in this National Stage				
application from the International E	sureau (PCT Kule 17.2(a))	s not received.				
* See the attached detailed Office action for	a list of the certified copie					
		•				
Attachment(s)						
1) Notice of References Cited (PTO-892)	D	rview Summary (PTO-413) per No(s)/Mail Date				
 2) Notice of Draftsperson's Patent Drawing Review (PTO-9 3) Information Disclosure Statement(s) (PTO-1449 or PTO/Paper No(s)/Mail Date 5/31/2002. 	SB/08) 5) 🔲 Not	ice of Informal Patent Application (PTO-152) er:				
Trademodi Office	ffice Action Summary	Part of Paper No./Mail Date 02052004				

Art Unit: 1753

Claim Objections

- 1. Claim 1 is objected to because of the following informality:
 - a) Claim 1, line 6: "by" should be -- with --.
- 2. Appropriate correction is required.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 6,331,235 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 3 implies a clinical sample. Claim 3 requires the BPD's to be

Page 3

Application/Control Number: 10/026,980

Art Unit: 1753

selected from BPD-MA, BPD-DA, and mixtures thereof. These BPD's are photosensitizers with clinical applications (col. 2, 11. 31-36 and col. 4, 11. 56-65).

- 5. Claim 2 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 3 of U.S. Patent

 No. 6,331,235 B1. Claim 1, from which Claim 2 depends, has been addressed above.

 Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 2 requires the capillary electrophoresis system to comprise a laser-induced fluorescence detection system.
- 6. Claim 3 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 6,331,235 B1. Claim 1, from which Claim 3 depends, has been addressed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 3 of U.S. Patent No. 6,331,235 B1 requires the BPDs to be selected from BPD-MA, BPD-DA, or mixtures thereof.
- 7. Claims 4-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-21, respectively, of U.S. Patent

¹ "The specification can always be used as a dictionary to learn the meaning of a term in the in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)." MPEP 804 II. B. 1., page 800-22, August 2001 ed,)

Page 4

Application/Control Number: 10/026,980

Art Unit: 1753

No. 6,331,235 B1. Claim 1, from which Claims 4-21 depend, has been addressed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the additional feature provided by each of claims 4-20 of the instant application is also provided by the claim of the same number in of U.S. Patent No. 6,331,235 B1.

Claim Rejections - 35 USC § 112

- 8. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:
 - a) Claim 1, line 10: "stereoisomers,." should be -- stereoisomers. --.
- 9. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 103

- 10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Art Unit: 1753

- 11. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
 - 1. Determining the scope and contents of the prior art.
 - 2. Ascertaining the differences between the prior art and the claims at issue.
 - 3. Resolving the level of ordinary skill in the pertinent art.
 - 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
- 12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
- 13. The pripor art rejections applied during the prosecution of U.S. application no. 09/321,893 are now applied to claims 1-21 of the instant application. During prosecution of U.S. application no. 09/321,893 Applicant averred in the response of March 22, 2001, 'Section 3.2 [of Dixon et al.] is directed to the separation of "atropisomers", which are not stereoisomers' (page 4 of the response) and "The atropisomers are not optical isomers" (page 5 of the amendment). Applicant relied, at

Art Unit: 1753

least in part, on the definition of "atropisomer" in the McGraw-Hill Dictionary of Scientific and Technical Terms. The examiner has reconsidered this argument and respectfully disagrees.

As Applicant stated in his response of March 22, 2001 in U.S. application 09/321,893, "atropisomer" is defined in the *McGraw-Hill Dictionary of Scientific and Technical Terms* as "one of two conformations of a molecule whose interconversion is slow enough to allow separation and isolation under predetermined conditions." However, "conformation" is defined in the same dictionary as "in a molecule, a specific orientation of the atoms that varies from other possible orientations by rotation or rotations about single bonds; generally in mobile equilibrium with other conformations of the same structure" and "stereoisomers" is defined as "compounds whose molecules have the same number and kind of atoms and the same atomic arrangement but differ in their spatial relationship." From these definitions, in Applicant's supporting reference, it follows that an atropisomer is a stereoisomer.

That an atropisomer is a stereoisomer is corroborated by other chemistry texts. Organic stereochemistry, Henri Kagan, John Wiley & Sons, 1978, on page 107, 'The name 'atropoisomerism' has been proposed to characterize the stereoisomers (enantiomers or diastereomers) which are the direct consequence of this [steric] hindrance of rotation." The Concise Encyclopedia of Chemistry, translated and revised by Mary Eagleson, Walter de Gruyter, 1994, defines "atropisomerism" as "a type of configurational isomerism which results when steric hindrance completely prevents rotation around a C-C single bond" and "configurational isomers are stereosiomers which

² McGraw-Hill Dictionary of Scientific and Technical Terms, online edition, last modified Sep. 30, 2003

Art Unit: 1753

cannot be interconverted by rotation of atoms or groups around a single bonds." In the *IUPAC Compendium of Chemical Terminology*, 2nd Edition (1997), "atropisomers" is defined as "a class of *conformers* which can be isolated as a separate *chemical species* which arise from restricted rotation about a single bond, e.g. *ortho*-substituted biphenyl, 1,1,2,2-tetra-butylethane" and a "conformer" is "one of a set of *stereoisomers*, each of which is characterized by a *conformation* to a distinct potential energy minimum."

Furthermore, that the atropisomers of Dixon et al. are stereoisomers may be seen in Figure 1 of Kaufamnn et al., "Separation of Rotational Isomers of Tetrakis(N-methyl-2-pyridimiumyl)porphyrin and Crystal Structure of $\alpha,\alpha,\alpha,\beta$ -(Tetrakis(N-methyl-2-pyridiniumyl)porphyrin)copper Hexacyanoferrate," *Inorg. Chem.*, 1995, 34, 5073-5079, which Dixon et al. cites (first paragraph in first column on page 373).

Thus, Applicant's assertions that an atropisomer is not a stereoisomer and in particular that the atropisomers separated by Dixon et al. are not stereoisomers are in error.

14. Claims 1, 3-13, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dixon et al. (("Capillary electrophoretic separation of cationic porphyrins", Journal of Chromatography A, 802 (1998), 367-380) in view of Jamieson et al. ("Preferential Uptake of Benzoporphyrin Derivative by Leukemic versus Normal Cells", Leukemia Research, 14(3), pp. 209-219), CAPLUS abstract of Wu et al. ("Separation of porphyrins using a γ -cyclodextrin stationary phase", J. Liq. Chromatogr., (1994), 1795), 1111-24),

³ ibid.

Art Unit: 1753

CAPLUS abstract of Fanali et al. ("The utility of cyclodextrins in capillary electrophoresis", J. Capillary Electrophor., (1994), 1(1), 72-8), Armstrong et al. ("Derivatized cyclodextrins immobilized on fused-silica capillaries for enantiomeric separations via capillaries for enantiomeric separations via capillary electrophoresis, gas chromatography, or supercritical chromatography", Anal. Chem. (1993), 65(8), 1114-17), and Yao et al. ("Optimization of separation of separation of porphyrins by micellar electrokinetic chromatography using the overlapping resolution mapping scheme", 637, (1993), 195-200).

Addressing claim 1. Dixon et al. teaches a method of separating stereoisomers of porphyrin derivatives (PDs) by a capillary electrophoresis system, which method comprises

injecting a sample containing PD stereisomers into a capillary electrophoresis system, and

separating the PD stereoisomers with the capillary electrophoresis system,

wherein the capillary inner diameter, capillary length, field strength, separation temperature, pH, buffer system, ionic strength, and organic solvent are selected to result in separation of PD stereoisomers.

See the abstract; 2.1 General methods on page 368; 2.2 Capillary electrophoresis beginning on page 368; 2.3 Centrifugal partition chromatography on page 370; and 3.2 Separation of atropisomers of TMPyP(2) beginning on page 372.

Dixon does not mention, (a) benzoporphyrin derivatives, (b) a "clincal' sample, and (c) a chiral selector.

Art Unit: 1753

As for benzoporphyrin derivatives, although benzoporphyrins are not mentioned, Dixon et al. does teach separating stereoisomers of porphyrin derivatives that have sixmembered aromatic ring substituents (Figure 1), which are analogous to benzoporphyrins and indeed can be construed as benzoporphyrin "derivatives." Also, Jamieson et al. teaches that benzoporphyrin derivatives, which are cytotoxic, have potential as anticancer compounds because they are preferentially taken up by leukemic cells over normal cells. See the abstract. It would have been obvious to one with ordinary skill in the art at the time the invention was made to modify the method of Dixon et al. so as to separate stereoisomers of benzoporphyrin derivatives because the porphyrin stereoisomers separated the Dixon et al. are analogous to benzophorphyrin derivatives, if not in fact benzoporphyrin derivatives, and as taught by Jamieson benzoporphyrin derivatives appear to have significant potential for treating cancer, which is a use Dixon et al. appreciated ("Cationic porphyrins ... have a wide variety of uses including ... as potential chemotherapeutic ... agents [I]ncreasing use is made of asymmetrically substituted members of this class in studies of ... anticancer activity ..." first paragraph of Introduction on page 367).

As for the benzoporphyrin stereoisomers being in a clinical sample, it would have been obvious to one with ordinary skill in the art at the time the invention was made to perform electrophoresis of benzoporphyrin stereoisomers in clinical samples because, as noted in the previous paragraph, benzoporphyrins may be useful as chemotherapeutic agents.

As for a chiral selector, Dixon et al. did not need one in the disclosed example.

Chiral selectors, for example cyclodextrins, were used at the time of the invention for

Art Unit: 1753

separating stereoisomers by electrophoresis. See Fanali and Armstrong. It was also known that a chiral selector, such as a cyclodextrin, would be useful in separating porphyrins. See Wu who also considers the effects of pH, ionic strength, and organic modifier. Barring evidence to the contrary, such as unexpected results, it would have been obvious to one with ordinary skill in the art at the time the invention was made to use a chiral selector because it is was known in the art that a chiral selector will enhance selectivity between structurally similar compounds, especially stereoisomers. Yao et al. clearly shows that optimizing the parameters of capillary electrophoresis separation of porphyrins was known at the time of the invention. See the abstract.

Addressing claim 3, it would have been obvious to one with ordinary skill in the art at the time the invention was made to electrophorese BPD-MA, BPD-DA, or mixtures thereof because as taught by Jamieson et al. these BPDs are useful in leukemia studies (the abstract and Figure 1).

Addressing claim 4, for baseline separation see in Dixon et al. Figure 4.

Addressing claims 5-7, for the claimed capillary dimensions see in Dixon the last paragraph in the second column on page 368, which discloses similar dimensions. Barring a contrary showing, optimizing electrophoresis parameters for better separation is obvious.

Art Unit: 1753

Addressing claims 8 and 9. for the claimed field strengths see in Dixon the last paragraph in the second column on page 369 and the first full column on page 373.

Addressing claims 10 and 11, see the first full sentence in the first column on page 370: "The column temperature was maintained around 20°C."

Addressing claims 12 and 13. Dixon discloses pH=4.0 (Figure 4). However, Dixon found that "the separation was independent of buffer pH." See the last paragraph in the first column on page 373. So, clearly Dixon recognized pH as a factor which may affect the quality of the separation. Using pH about 9.6 or 9.2 to separate porphyrins was known at the time of the invention. See Figure 4 in Yao. It would have been obvious to one with ordinary skill in the art at the time the invention was made to select a pH that will enhance the separation.

Addressing claim 20, for DMF see the last two sentences in the first column of page 196 in Yao, which teaches using DMF to optimize separation of porphyrins.

15. Claims 2, 17-19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dixon et al. ("Capillary electrophoretic separation of cationic porphyrins", Journal of Chromatography A, 802 (1998), 367-380) in view of Jamieson et al. ("preferential Uptake of Benzoporphyrin Derivative by Leukemic versus Normal Cells", Leukemia Research, 14(3), pp. 209-219), CAPLUS abstract of Wu et al. ("Separation of porphyrins using a γ-

Art Unit: 1753

cyclodextrin stationary phase", J. Liq. Chromatogr., (1994), 1795), 1111-24), CAPLUS abstract of Fanali et al. ("the utility of cyclodextrins in capillary electrophoresis", J. Capillary Electrophor., (1994), 1(1), 72-8), and Armstrong et al. ('Derivatized cyclodextrins immobilized on fused-silica capillaries for enantiomeric separations via electrophoresis, gas capillary enantiomeric separations via capillaries for chromatography, or supercritical chromatography", Anal. Chem. (1993), 65(8), 1114-17), and Yao et al. ("Optimization of separation of separation of porphyrins by micellar electrokinetic chromatography using the overlapping resolution mapping scheme", 637, (1993), 195-200). as applied to claims 1, 3-13, 20 above, and further in view of Wu et al. ("Recent developments in Porphyrin separations using Capillary Electrophoresis with Native Fluorescence Detection", Journal of Liquid Chromatography, 17(9), 1917-1927 (1994)).

Addressing claim 2. Dixon et al. as modified by Jamieson et al., Wu et al. (CAPLUS), Fanali et al., and Armstrong et al. does not mention a laser-induced fluorescence detection system, although one may reasonably infer such a detection system because no dyes were used and UV-Vis spectra were obtained. See sections 2.1 General methods and 2.2 Capillary electrophoresis on page 368 and Figure 4 of Dixon. In any event using a laser-induced fluorescence detection system to detect isomers of porphyrins was known in the art as shown by Wu et al. (J. Liq. Chromatog.), for example. See the abstract. It would have been obvious to one with ordinary skill in the art at the time the invention was made to use a laser-induced fluorescence (LIF) detection system in the invention as taught by Wu et al. in the invention of Dixon et al. as modified by

Art Unit: 1753

Jamieson et al., Wu et al. (CAPLUS), Fanali et al., and Armstrong et al. because as taught by Wu et al. (J. Liq. Chromatog.), "[c]urrently, LIF is one of the most sensitive methods for CE and detection limits under 1000 molecules have been reported." See the first full paragraph on page 1918.

Addressing claims 17-19. Dixon et al. as modified by Jamicson et al., Wu et al. (CAPLUS), Fanali et al., and Armstrong et al. does not mention using a bile salt such as cholate, especially sodium cholate as a chiral selector. Yao teaches that bile salts were known in the art at the time of the invention as a chiral selector: "[b]ile salt micelles have been successfully applied to the resolution of optical isomers in HPLC and MEKC [micellar electrokinetic chromatography]." See the first full paragraph on page 1918. Yao had found that sodium cholate is useful in separating porphyrin isomers that are important for photodynamic therapy (Figure 3 and last paragraph on page 1923). Barring evidence to the contrary, such as unexpected results, it would have been obvious to one with ordinary skill in the art at the time the invention was made to use a bile salt such as cholate, especially sodium cholate as a chiral selector because as shown by Yao such a chiral selector offers acceptable separations of porphyrin isomers under certain conditions.

Addressing claim 21. Dixon et al. as modified by Jamieson et al., Wu et al. (CAPLUS), Fanali et al., and Armstrong et al. does not mention using acetonitrile as the organic solvent. Yao et al. teaches that using a bile salt in combination with acetonitrile

Art Unit: 1753

is useful in separating porphyrin isomers (Figure 3 and last paragraph on page 1923). Barring evidence to the contrary, such as unexpected results, it would have been obvious to one with ordinary skill in the art at the time the invention was made to use acetonitrile as taught by Yao et al. in the invention of Dixon et al. as modified by Jamieson et al., Wu et al. (CAPLUS), Fanali et al., and Armstrong et al. because as shown by Yao et al. acetonitrile offers acceptable separations of porphyrin isomers under certain conditions.

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over 16. Dixon et al. ("Capillary electrophoretic separation of cationic porphyrins", Journal of Chromatography a, 802 (1998), 367-380) in view of Jamieson et al. ("preferential Uptake of Benzoporphyrin Derivative by Leukemic versus Normal Cells", Leukemia Research, 14(3), pp. 209-219), CAPLUS abstract of Wu et al. ("Separation of porphyrins using a γcyclodextrin stationary phase", J. Liq. Chromatogr., (1994), 1795), 1111-24), CAPLUS abstract of Fanali et al. ("the utility of cyclodextrins in capillary electrophoresis", J. Capillary Electrophor., (1994), 1(1), 72-8), and Armstrong et al. ("Derivatized cyclodextrins immobilized on fused-silica capillaries for enantiomeric separations via separations via capillary electrophoresis, capillaries for enantiomeric chromatography, or supercritical chromatography", Anal. Chem. (1993), 65(8), 1114-17), and Yao et al. ("Optimization of separation of separation of porphyrins by micellar electrokinetic chromatography using the overlapping resolution mapping scheme", 637, (1993), 195-200) as applied to claims 1, 3-13, 20 above, and further in view of Chan et al.

Art Unit: 1753

("Capillary electrophoresis analysis of polyhaematoporphyrin, a photosensitizer used in photodynamic therapy", Journal of Chromatography, 636 (1993) 171-178).

Addressing claim 14. Dixon et al. as modified by Jamieson et al., Wu et al. (CAPLUS), Fanali et al., and Armstrong et al. does not mention using borate in the buffer, but does teach using phosphate(Figure 4). Chan teaches separating porphyrins under various conditions. In particular, he presents results that allow comparison of separations with phosphate to separations with borate (Figures 4 and 5). Barring evidence to the contrary, such as unexpected results, it would have been obvious to one with ordinary skill in the art at the time the invention was made to use borate as a buffer because as shown by Chan it offers acceptable separations under certain conditions. In other words, it would have been obvious to use a buffer system known to enhance porphyrin separations.

Addressing claims 15 and 16. The selection of ionic strength is just a matter of optimizing the separation. Consider Figure 1 in Yao.

Art Unit: 1753

Information Disclosure Statement

Page 16

17. Applicant is requested to provide a copy of the Stalcup et al. article cited in the

IDS of May 31, 2002, which is item no. 42, under "Other Documents".

18. Any inquiry concerning this communication or earlier communications from the

examiner should be directed to ALEX NOGUEROLA whose telephone number is (571)

272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number

for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business

Center (EBC) at 866-217-9197 (toll-free).

alex Noguerola

02/09/04

Prinary Examiner .

TC.1753